

INVENT COOPERATION TRE

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

Date of mailing (day/month/year)
03 May 2000 (03.05.00)

From the INTERNATIONAL BUREAU

To:

ELLIS-JONES, Patrick, George,
Armine
J.A. Kemp & Co.
14 South Square
Gray's Inn
London WC1R 5LX
ROYAUME-UNI

Applicant's or agent's file reference
N.75052C PEJ

IMPORTANT NOTIFICATION

International application No.
PCT/GB99/03133

International filing date (day/month/year)
21 September 1999 (21.09.99)

1. The following indications appeared on record concerning:

the applicant the inventor the agent the common representative

Name and Address
ISIS INNOVATION LIMITED
2 South Parks Road
Oxford OX1 3UB
United Kingdom

| | |
|----------------------------|--------------------------|
| State of Nationality GB | State of Residence GB |
| Telephone No. | |
| Facsimile No. | |
| Teleprinter No. | |

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person the name the address the nationality the residence

Name and Address
ISIS INNOVATION LIMITED
Ewert House
Ewert Place
Summertown
Oxford OX2 7BZ
United Kingdom

| | |
|----------------------------|--------------------------|
| State of Nationality GB | State of Residence GB |
| Telephone No. | |
| Facsimile No. | |
| Teleprinter No. | |

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

| | |
|---|---|
| <input checked="" type="checkbox"/> the receiving Office | <input type="checkbox"/> the designated Offices concerned |
| <input type="checkbox"/> the International Searching Authority | <input checked="" type="checkbox"/> the elected Offices concerned |
| <input checked="" type="checkbox"/> the International Preliminary Examining Authority | <input type="checkbox"/> other: |

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Yolaine CUSSAC

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

| | |
|--|--|
| Date of mailing (day/month/year) 03 May 2000 (03.05.00) | |
| International application No. PCT/GB99/03133 | Applicant's or agent's file reference N.75052C PEJ |
| International filing date (day/month/year) 21 September 1999 (21.09.99) | Priority date (day/month/year) 21 September 1998 (21.09.98) |
| Applicant DOBSON, Christopher, Martin | |

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

24 March 2000 (24.03.00)

in a notice effecting later election filed with the International Bureau on:

2. The election was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Yolaine CUSSAC |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

PATENT COOPERATION TREATY

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REC'D 21 DEC 2000

WIPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | | |
|--|--|--|---|
| Applicant's or agent's file reference N.75052CPEJ | FOR FURTHER ACTION | | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/GB99/03133 | International filing date (day/month/year) 21/09/1999 | Priority date (day/month/year) 21/09/1998 | |
| International Patent Classification (IPC) or national classification and IPC C12N9/12 | | | |
| Applicant ISIS INNOVATION LIMITED et al. | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> | | | |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application | | | |

| | |
|--|--|
| Date of submission of the demand 24/03/2000 | Date of completion of this report 19.12.2000 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized officer Stolz, B Telephone No. +49 89 2399 8416 |



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/03133

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).:*)

Description, pages:

1-32 as originally filed

Claims, No.:

1-32 as originally filed

Drawings, sheets:

1/13-13/13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of: .

- the description, pages:
- the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/03133

the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.

claims Nos. 1-3 (partly), 4-9, 10-32(partly).

because:

the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos. cf. above.

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

the written form has not been furnished or does not comply with the standard.

the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 10, 18-21, 26, 28-32

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/03133

No: Claims 1-3, 11-17, 22-25, 27

Inventive step (IS) Yes: Claims 10, 28-32
No: Claims 1-3, 11-27

Industrial applicability (IA) Yes: Claims 1-3, 9-32
No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03133

1. Reasoned statement

1.1. As the ISR has only been carried out as far as naturally occurring amyloid fibres are concerned, i.e. claims 1 to 3, and 10 to 32, this report has only been written with regard to these.

1.2. Novelty (Art. 33(2) PCT)

Amyloid fibrils and fragments thereof have been intensely studied in the art (Malinchik et al., Castāno et al., Kirschner et al., and US 4,666,829, all cited in the ISR). An amyloid fibril derived from SH3 domains has also been described by Guijarro et al.. These fibrils are described as ranging from 6 to 10 nm in diameter. They were gold labelled (Castāno et al) and Guijarro et al used pH 2.0 for their production. Since A β comprises a lysine residue (not to mention the N- and C-terminus), it comprises at least one functional group capable of binding a reactant. As a consequence, claims 1 to 3, 11 to 17, 22 to 25, and 27 are considered to lack novelty.

1.3. Inventive step (Art. 33(3) PCT)

The process steps specified in claims 18 to 21, and 26 are considered to represent obvious modifications to the process of claim 17.

The claimed medical and non-medical uses of amyloid fibrils have neither been described in the available prior art nor are they derivable from this prior art in an obvious way.

2. Certain observations

2.1. The term amyloid fibril is not clear because its meaning is being expanded to include any protein self-assembling into fibril-like structures. Traditionally however, the term has been used to characterize peptides associated with specific pathogenic states. Thus, the scope of protection cannot be established unambiguously.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03133

- 2.2. The terms "substantially free of" (claim 1), "pharmaceutically active" (claim 10), and "an acceptable time" (claim 17) are also open to interpretation. Even sodium chloride can be pharmaceutically active.

PATENT COOPERATION TREATY
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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|--|
| Applicant's or agent's file reference N. 75052CPEJ | FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | |
| International application No. PCT/GB 99/ 03133 | International filing date (day/month/year) 21/09/1999 | (Earliest) Priority Date (day/month/year) 21/09/1998 |
| Applicant ISIS INNOVATION LIMITED et al. | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of **8** sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
 - contained in the international application in written form.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority in written form.
 - furnished subsequently to this Authority in computer readable form.
 - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. _____

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 99/03133

B x I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 31-32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheets

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

(1-3, 10, 32) - partially

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: (1-3,10-32) - partially

A naturally occurring amyloid fibril substantially free of other protein, wherein the fibril comprises the A-beta peptide associated with Alzheimer's disease.

Pharmaceutical compositions, complexes with metals, variants carrying more functional groups capable of binding reactants. Uses as a plastic or in electronic or catalysis, therapeutic uses. A method to prepare said fibril.

2. Claims: (1-3,10-32) - partially

Idem as subject-matter 1, but wherein the fibril comprises the prion protein associated with the transmissible spongiform encephalopathies.

3. Claims: (1-3,10-32) - partially

Idem as subject-matter 1, but wherein the fibril comprises the islet-associated polypeptide associated with type II diabetes.

4. Claims: (1-3,10-32) - partially

Idem as subject-matter 1, but wherein the fibril comprises the transthyretin and fragments thereof associated with familial amyloidotic polyneuropathy.

5. Claims: (4-32) - partially

A non-naturally occurring amyloid fibril comprising a derivative or amino acid variant of an SH3 domain of a p85-alpha subunit of bovine phosphatidyl-inositol 3-kinase

A composite fibril, further comprising a (non variant) SH3 domain of a p85-alpha subunit of bovine phosphatidylinositol 3-kinase.

Pharmaceutical compositions, complexes with metals, variants carrying more functional groups capable of binding reactants. Uses as a plastic or in electronic or catalysis, therapeutic uses. Methods to prepare said fibril.

6. Claims: (4-32) - partially

Idem as subject-matter 5, but wherein the fibril comprises a human muscle acylphosphatase.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. Claims: (4-32) - partially

Idem as subject-matter 5, but wherein the fibril comprises bovine insulin.

8. Claims: (4-32) - partially

Idem as subject-matter 5, but wherein the fibril comprises a protein corresponding to the first two (CspB-1), the first three (CspB-2) or the last two (CspB-3) beta strands of CspB.

9. Claims: (4-32) - partially

Idem as subject-matter 5, but wherein the fibril comprises the wild type human carboxypeptidase A2.

10. Claims: (17-26) - partially

As far as not covered by inventions 1-9:

A process for preparing a fibril which comprises preparing a solution comprising a protein, said solution being in a state so that nucleation and fibril growth will occur over an acceptable time, and allowing fibril growth to take place.

INTERNATIONAL SEARCH REPORT

PCT/GB 99/03133

B x III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Amyloid fibrils substantially free of other protein are described, along with methods to obtain them and biophysical characterization.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03133

A. CLASSIFICATION OF SUBJECT MATTER

| | | | | | |
|-------|-----------|-----------|-----------|-----------|-----------|
| IPC 7 | C12N9/12 | C12N9/14 | C12N9/48 | C07K14/32 | C07K14/47 |
| | C07K14/62 | C07K1/113 | A61K38/16 | A61K38/17 | A61K38/28 |
| | C08K/00 | | | | |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K A61K C08K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| X | <p>MALINCHIK S.B. ET AL.: "Structural analysis of Alzheimer's beta(1-40) amyloid: protofilament assembly of tubular fibrils" BIOPHYS. J., vol. 74, January 1998 (1998-01), pages 537-545, XP002127772 the whole document</p> <p>---</p> <p>-/-</p> | 1-3, 10-32 |

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

17 January 2000

12.04.00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Galli, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03133

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|--|-----------------------|
| X | CASTANO E M ET AL: "IN VITRO FORMATION OF AMYLOID FIBRILS FROM TWO SYNTHETIC PEPTIDES OF DIFFERENT LENGTHS HOMOLOGOUS TO ALZHEIMET'S DISEASE BETA-PROTEIN" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, US, ACADEMIC PRESS, SAN DIEGO, CA, vol. 141, no. 2, 1986, page 782-789 XP002127777 ISSN: 0006-291X the whole document --- | 1-3, 10-32 |
| X | KIRSCHNER D.A. ET AL.: "Synthetic peptide homologous to beta protein from Alzheimer disease forms amyloid-like fibrils in vitro" PROC. NATL. ACAD. SCI. USA, vol. 84, October 1987 (1987-10), pages 6953-6957, XP002127773 the whole document --- | 1-3, 10-32 |
| A | US 4 666 829 A (GLENNER GEORGE G ET AL) 19 May 1987 (1987-05-19) the whole document --- | 1-3, 10-32 |
| A | TJERNBERG L O ET AL: "CONTROLLING AMYLOID BETA-PEPTIDE FIBRIL FORMATION WITH PROTEASE-STABLE LIGANDS" JOURNAL OF BIOLOGICAL CHEMISTRY, US, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, vol. 272, no. 19, 9 May 1997 (1997-05-09), page 12601-12605 XP002050230 ISSN: 0021-9258 the whole document --- | 1-3, 10-32 |
| A | WO 97 15195 A (TRANSKARYOTIC THERAPIES INC) 1 May 1997 (1997-05-01) abstract --- | 1-3, 10-32 |
| A | US 5 171 574 A (KUBERASAMPATH THANGAVEL ET AL) 15 December 1992 (1992-12-15) abstract --- | 1-3, 10-32 |
| A | WO 97 15933 A (HOECHST CELANESE CORP) 1 May 1997 (1997-05-01) abstract page 5, line 28 - line 31 page 10, line 10 - line 21 claims 1-27 --- | 1-3, 10-32 |

-/-

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 99/03133

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| X | GUIJARRO J.I. ET AL.: "Amyloid fibril formation by an SH3 domain" PROC. NATL. ACAD. SCI. USA, vol. 95, April 1998 (1998-04), pages 4224-4228, XP002127774 cited in the application the whole document ----- | 1 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03133

| Patent document cited in search report | Publication date | Patent family member(s) | | Publication date |
|--|------------------|-------------------------|-------|------------------|
| US 4666829 | A 19-05-1987 | CA 1268131 | A | 24-04-1990 |
| ----- | ----- | ----- | ----- | ----- |
| WO 9715195 | A 01-05-1997 | US 5965125 | A | 12-10-1999 |
| | | AU 706563 | B | 17-06-1999 |
| | | AU 7474496 | A | 15-05-1997 |
| | | EP 0917428 | A | 26-05-1999 |
| | | JP 2000501299 | T | 08-02-2000 |
| | | NO 981859 | A | 24-06-1998 |
| ----- | ----- | ----- | ----- | ----- |
| US 5171574 | A 15-12-1992 | US 5011691 | A | 30-04-1991 |
| | | US 4975526 | A | 04-12-1990 |
| | | AT 167486 | T | 15-07-1998 |
| | | AU 648997 | B | 12-05-1994 |
| | | AU 6648190 | A | 16-05-1991 |
| | | CA 2027259 | A | 18-04-1991 |
| | | CA 2042577 | A | 18-04-1991 |
| | | DE 69032424 | D | 23-07-1998 |
| | | DE 69032424 | T | 04-02-1999 |
| | | EP 0448704 | A | 02-10-1991 |
| | | ES 2118723 | T | 01-10-1998 |
| | | GR 3027722 | T | 30-11-1998 |
| | | JP 10114673 | A | 06-05-1998 |
| | | JP 2845346 | B | 13-01-1999 |
| | | JP 4502336 | T | 23-04-1992 |
| | | WO 9105802 | A | 02-05-1991 |
| | | US 5468845 | A | 21-11-1995 |
| | | US 5714589 | A | 03-02-1998 |
| | | US 5958441 | A | 28-09-1999 |
| | | US 5863758 | A | 26-01-1999 |
| | | US 5266683 | A | 30-11-1993 |
| | | US 5344654 | A | 06-09-1994 |
| | | US 5354557 | A | 11-10-1994 |
| | | AT 142644 | T | 15-09-1996 |
| | | AT 134647 | T | 15-03-1996 |
| | | AT 124051 | T | 15-07-1995 |
| | | AU 628050 | B | 10-09-1992 |
| | | AU 3444989 | A | 03-11-1989 |
| | | AU 618357 | B | 19-12-1991 |
| | | AU 3530589 | A | 03-11-1989 |
| | | AU 627850 | B | 03-09-1992 |
| | | AU 5174790 | A | 26-09-1990 |
| | | CA 1338663 | A | 22-10-1996 |
| | | DE 68925773 | D | 04-04-1996 |
| | | DE 68925773 | T | 17-10-1996 |
| | | DE 68927153 | D | 17-10-1996 |
| | | DE 68927153 | T | 06-03-1997 |
| | | DE 69020254 | D | 27-07-1995 |
| | | DE 69020254 | T | 25-01-1996 |
| | | DK 411105 | T | 30-10-1995 |
| | | EP 0372031 | A | 13-06-1990 |
| | | EP 0362367 | A | 11-04-1990 |
| | | EP 0411105 | A | 06-02-1991 |
| | | EP 0714665 | A | 05-06-1996 |
| | | EP 0723013 | A | 24-07-1996 |
| | | ES 2074158 | T | 01-09-1995 |
| | | JP 2933867 | B | 16-08-1999 |
| | | JP 8336390 | A | 24-12-1996 |
| | | JP 2869381 | B | 10-03-1999 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03133

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|--|------------------|-------------------------|------------------|
| US 5171574 A | | JP 8322570 A | 10-12-1996 |
| WO 9715933 A | 01-05-1997 | US 5762830 A | 09-06-1998 |

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING
SUBMISSION OR TRANSMITTAL
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

ALC

From the INTERNATIONAL BUREAU

To:

ELLIS-JONES, Patrick, George,
Armine
J.A. Kemp & Co.
14 South Square
Gray's Inn
London WC1R 5LX
ROYAUME-UNI

J. A. KEMP & CO

24 NOV 1999

Action by

| | |
|--|------------------------|
| Date of mailing (day/month/year) 17 November 1999 (17.11.99) | IMPORTANT NOTIFICATION |
| Applicant's or agent's file reference N.75052C PEJ | |
| International application No. PCT/GB99/03133 | |
| International publication date (day/month/year) Not yet published | |

International filing date (day/month/year)
21 September 1999 (21.09.99)Priority date (day/month/year)
21 September 1998 (21.09.98)Applicant
ISIS INNOVATION LIMITED et al

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

| <u>Priority date</u> | <u>Priority application No.</u> | <u>Country or regional Office or PCT receiving Office</u> | <u>Date of receipt of priority document</u> |
|--------------------------|---------------------------------|---|---|
| 21 Sept 1998 (21.09.98) | 9820555.2 | GB | 25 Oct 1999 (25.10.99) |
| 30 Marc 1999 (30.03.99) | 60/126,871 | US | NR |
| 29 April 1999 (29.04.99) | 9909927.7 | GB | 25 Oct 1999 (25.10.99) |

APG

PATENT COOPERATION TREATY

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

From the INTERNATIONAL BUREAU

To: ELLIS-JONES, Patrick, George

Armine

J.A. Kemp & Co

14 South Square

Gray's Inn

London WC1R 5LX

ROYAUME-UNI

J. A. KEMP & Co

REC'D 10 APR 2000

Action by.....

Date of mailing (day/month/year)
30 March 2000 (30.03.00)Applicant's or agent's file reference
N.75052C PEJInternational application No.
PCT/GB99/03133International filing date (day/month/year)
21 September 1999 (21.09.99)Priority date (day/month/year)
21 September 1998 (21.09.98)Applicant
ISIS INNOVATION LIMITED et al

IMPORTANT NOTICE

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
JP,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
EP

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 30 March 2000 (30.03.00) under No. WO 00/17328

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/I/B/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No. (41-22) 740.14.35

Form PCT/I/B/308 (July 1996)

Authorized officer

J. Zahra

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